Cell Mechanics and Motility I

869-Pos Board B624

Fibroblast Phenotype Transformation by Cocultured Cancer Epithelial Cells

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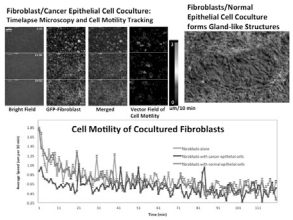
Cancer-associated fibroblasts (CAFs) play a critical role in tumor progression and are associated with high-grade malignancy and hindrance of anti-cancer pharmacotherapy. While it is observed that CAFs exhibit myofibroblast-like phenotypes and are highly contractile, the process by which normal fibroblasts (NFs) are transformed into CAFs is yet to be elucidated. To gain insight about this process, we constructed a coculture system where GFP-labeled NIH3T3 fibroblasts were cocultured with cancer or normal mammary gland epithelial cells, respectively. The dynamic interactions between fibroblasts and epithelial cells were recorded by timelapse microscopy for 20 hours upon seeding and tracked using image correlation analysis. The results showed that fibroblasts cocultured with cancer epithelial cells exhibited different cell mobility profiles compared to normal controls. Furthermore, pattern recognition-based image analysis revealed that fibroblasts/cancer epithelial cell coculture produced lesion-like structures whereas the control coculture produced gland-like structures. Fibroblasts were then microdissected from the cocultures to examine the expression level of various CAF-related proteins in Western blot. The results showed that myosin II phosphorylation is significantly upregulated in fibroblasts co-cultured with cancer epithelial cells, indicating NF-CAF transformation can occur within 20 hours after NFs are in contact with cancer cells.



870-Pos Board B625

Endothelial Surface Protrusion by a Point Load

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During leukocyte rolling on the endothelium, two types of mechanical deformation, surface protrusion and membrane tether extraction, occur consecutively on leukocytes. Both surface protrusion and tether extraction of leukocytes stabilize leukocyte rolling, but for tether extraction to initiate, a crossover force has to be overcome in advance. Tethers can also be extracted from endothelial cells (ECs), but whether there exists surface protrusion before tether extraction from ECs is still unknown. In this study, we found that surface protrusion did exist when a point force was imposed on an endothelial cell. Both the protrusional stiffness and the crossover force of EC surface protrusion were dependent on the force loading rate, but neither of them was dependent on tumor necrosis factor α stimulation. The effects of latrunculin treatment, α-actinin knockdown, and temperature were also studied. Theoretically, a three-parameter solid model was used to simulate EC surface protrusion and all material constants were calculated. When a neutrophil was employed to impose the pulling force on the EC, simultaneous surface protrusion from both cells occurred and it can be modeled as two ''springs'' connected in series. Therefore, EC surface protrusion is an integral aspect of leukocyte rolling and it is essential to be considered when leukocyte rolling stability is studied systematically.

871-Pos Board B626

Probing Collective Migration of a Complex Multi-Cellular Embryonic Tissue Through Novel 3D Bioetching

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Embryonic development consists of a complex series of cell signaling, cell migration and cell differentiation processes that are coordinated during morphogenesis. Collective cell sheet migration is an important process that sculpts the shape of an organism and its internal tissues during early development. Embryonic development and tissue self-assembly requires the integration of cell movements within multiple cell layers composed of different cell types. Considering the important role cell mechanics plays in tissue self-assembly it is surprising that little is known about the mechanical response of the multi-layer tissues to chemical cues. One of the reasons of this knowledge gap is the lack of the technologies to analyze the individual responses of epithelial and mesenchymal cell sheets in a multi cell layer tissue to mechanical cues. To investigate the processes that guide collective movements of multiple cell layers our group has focused on developing a novel microfluidic technique capable of producing complex patterns of laminar multicellular structures. We call this technique ''3D tissue-etching'' by analogy with the silicon micromachining techniques used to fabricate 3D structures in the MEMS field. We use tissue etching to shape a complex multi-layered embryonic tissue and explore the dynamic collective responses of epithelial and mesenchymal cells in a single tissue. We use a custom-designed microfluidic control system to deliver a range of tissue etching reagents over Animal Cap tissues of Xenopus laevis. Using etching, we produce free-edges of epithelial cells over mesenchymal cells and free-edges of mesenchymal cells. This allows us to study acute mechanical and behavioral response of intact epithelial and mesenchymal cell sheets to removal of neighboring or overlying tissues. The ability to control the multicellular tissues will have high impact in tissue engineering and regeneration applications in bioengineering and medicine.

872-Pos Board B627

Contractile Stress and Morphogen Diffusion in Developing Cell Assemblies

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A key feature of growth and pattern formation of cell assemblies in embryos is that the steady-state diffusion profile of the signaling morphogen molecules scales with the size of the embryo[1]. Recent research[2] has suggested biochemical mechanisms used by the embryo to achieve such scaling. However many of the processes involved in development are mechanical[3] in nature. In particular, the elastic forces due to cytoskeletal contractility are by their very nature, long-ranged[4], and could facilitate global effects in the pattern forming processes. As a first-step, we study a model that couples the morphogens to the "mechanical state" of the cells. In our model, the contractility profile decreases as a power law, instead of decaying exponentially (as expected for systems with local interactions) and is thus sensitive to the system boundaries. The effect of the elastic interactions on the diffusive behavior of morphogens is more subtle. We consider several possible models and boundary conditions for the effects of elasticity on diffusion in a finite system. Specific boundary conditions, such as stress-free boundary with a concentration fixed by biochemical feedback at one end, can lead to morphogen profiles that indeed scale with the size of the embryo.

[1] De Robertis, E. M., *Nature Rev. Mol. Cell Biol.***7**, 296-302 (2006).
[2] Ben-Zvi, D., Shilo, B. Z., Fainsod, A., & Barkai, N., *Nature***453**, 1205-1211 (2008).
[3] Forgacs, G and Newman A., *Biological Physics of the Developing Embryo*, (Cambridge University Press, 2005).
[4] Schwarz, U. S. & Safran, S. A., *Phys. Rev. Lett.***88**, 048102 (2002).

873-Pos Board B628

Probing Mechanosensitivity of 3T3 Fibroblasts on Biomembrane-Mimicking Cell Substrates

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BPS meeting 2014 spring

Cells are frequently anchorage-dependent and respond sensitively to changes in substrate viscoelasticity. Cellular mechano-sensitivity has been traditionally explored using polymeric gels of adjustable crosslinking density with immobilized linkers. However, such polymeric films can be prone to substrate artifacts affecting linker density and cell spreading/migration. Here, we show that cellular mechanosensitivity can also be probed using polymer-tethered lipid bilayers comprised of phospholipids and lipopolymers with specific cell-substrate linkers. In this biomembrane-mimicking supramolecular assembly, substrate viscoelasticity can be varied either by modification of bilayer number in a multi-bilayer stack or via control of lipopolymer density (without altering bilayer number). Characteristics of fibroblast cellular mechanosensitivity are analyzed in terms of: cell morphology,